UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,064	12/12/2003	Veronique Barban	API-02-14-US	1266

7590 02/08/2007

Patrick J. Halloran
Aventis Pasteur
Knerr Building
Swiftwater, PA 18370

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,064	BARBAN ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 29-34* is/are pending in the application.

4a) Of the above claim(s) *1-14,16,17,19-21 and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,18,22,23 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application is now pending in view of the petition to revive, granted on December 5, 2006. Claims 1-26 and 29-34 are pending in view of the amendment filed October 23, 2006. The elected invention reads on claims 15, 18, 22, 23 and 29-34, drawn to ALVAC viruses and compositions thereof. Claims 1-14, 16, 17, 19-21 and 24-26 remain withdrawn from consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected subject matter.

2. The following objection and rejections are withdrawn:

- The objection to claim 18 for depending from itself is withdrawn in view of Applicant's amendment.
- The rejection of claim 18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, is withdrawn in view of Applicant's amendment.
- The rejection of claims 15, 18, 22, 23 and 29-34 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn in view of Applicant's assurance that evidence that a deposit has been made under the Budapest Treaty will be supplied before the date of issuance of any patent resulting from this application. (The rejection was made because, although ALVAC has been deposited at the ATCC, it does not appear to be publicly available; and, deposit of ALVAC(2) does not appear to have been deposited in a recognized deposit facility. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant or someone associated with the patent owner who is in a position to make

such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.)

Claims Summary

3. The claims are drawn to a composition comprising either ALVAC (Albany vaccine), a canarypoxvirus, or ALVAC(2), which differs from ALVAC in that the genome comprises the vaccinia E3L and K3L genes under the control of vaccinia promoters (specification, page 4, last paragraph). The claims are constructed as product-by-process claims. Product-by-process claims are treated only with regard to the structural components present in the end product. The viruses are produced by a method comprising the steps of infecting one or more avian embryonic stem cells with an ALVAC virus, cultivating the infected avian embryonic stem cells to produce the virus, and isolating the virus. In another method production, the ALVAC virus comprises at least one exogenous nucleotide sequence encoding a human tumor antigen, an antigen derived from a human pathogen, or a fragment thereof. Avian embryonic stem cells are then infected and cultivated to produce the virus. The virus is harvested and then, i) inactivated, ii) supplemented with a pharmaceutically acceptable carrier or diluent, iii) supplemented with an adjuvant, or iv) lyophilized.

Specifically, the exogenous DNA sequence within the ALVAC or ALVAC(2) genome encodes a bacterial, fungal or viral antigen. The genome further comprises exogenous DNA encoding a co-stimulatory molecule, such as human B7.1.

The avian embryonic stem cells are EB1 or EB14 cells. The specification discloses that EB1 and EB14 cells (as described in FR02/02945 and WO 03/07661) were obtained from chick embryos at very early steps of embryogenesis and exhibit a stem cell phenotype (page 5, second paragraph). The cells are not genetically modified in their native state and grow in suspension. In one embodiment, the cells are EB1 cells obtained from VIVALIS SA (France; FR02/02945 and WO 03/07661). In a second embodiment, the cells are EB14 cells obtained from VIVALIS SA (FR02/02945 and WO 03/07661).

Claim Objections

4. (*New Objections*) Claims 15, 18, 22, 23 and 29-34 are objected to for the following informalities:

- Claim 15 recites a grammatical error, "(a) infecting one or mores avian embryonic stem cells" [emphasis added].
- Claims 15, 18, 22, 23 and 29-34 recite, "A composition comprising an ALVAC or ALVAC(2) virus produced by a method comprising the steps of (a) infecting avian embryonic stem cells with an ALVAC virus". It appears that Applicant intends for the embryonic stem cells to be infected with either ALVAC or ALVAC(2), depending on the virus desired for production. Correction is required for proper antecedent basis.

Claim Rejections - 35 USC § 112

5. (*New Rejection*) Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that EB1 and EB14 cells are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of these cells. See 37 CFR 1.802.

The specification discloses that EB1 and EB14 cells may be obtained from VIVALIS SA (France; FR02/02945 and WO 03/07661). However, the cells do not appear to be publicly available. One cannot practice the invention claim 34 without access to these cell lines. Therefore, access to EB1 and EB14 is required to practice the invention. The specification does not provide a repeatable method for obtaining these cells without access to the cells, and they do not appear to be readily available material.

Deposit of EB1 and EB14 in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to

make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

Claim Rejections - 35 USC § 102

6. Claims 15, 18, 22, 23, 29-31 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Paoletti *et al.* (US 5,833,975, "Paoletti"). The claims are summarized above.

Paoletti discloses canarypox viruses expressing tumor-associated antigen DNA (abstract). Specifically, the vector is ALVAC or ALVAC(2) (see instant specification, page 4, lines 28-30). The vectors are inactivated and administered with carriers (col. 8, lines 21-24, and col. 13, lines 27-47). Other genes are used in the vectors besides tumor antigens. Paoletti discloses the use of DNA from pathogens (col. 8, lines 34-46). Regarding the limitations in the claims as to their method of production, these limitations do not render the claims patentably distinct from the products disclosed by Paoletti. The end products are expected to be the same: an ALVAC or ALVAC(2) virus comprising an exogenous gene that encodes an antigen from a tumor or an antigen from a pathogen.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the assertion that the use of avian embryonic stem cells yields ALVAC and ALVAC(2) compositions having more desirable profiles than previously described. Particularly, the methods of Paoletti rely on the use of chicken embryo

fibroblasts to produce ALVAC (Paoletti, col. 16, lines 28-37). Applicant points to Appendix A, evidence that those of skill in the art have noted that the methods described in the instant claims provide a "safer...alternative to the use of...chicken primary embryonic fibroblasts for the production of a large amount of viral vectors and viruses for the manufacture of viral vaccines, such as poxviruses...." Applicant argues that the instantly claimed products have significant structural and functional advantage over previously available products.

In response to Applicant's arguments, the Office has considered Appendix A. Appendix A does not provide any specifics regarding the structural and functional differences between poxviruses produced in CEF cultures versus avian embryonic stem cells cultures. Appendix A only indicates that the use of avian embryonic stem cells cultures is safer. Safer culturing methods do not render the final products any different than culturing in CEF cells. Applicant does not appear to have any evidence that the ALVAC and ALVAC(2) viruses produced in CEF cells are any different (structurally and functionally) than the instantly claimed viruses. There does not appear to be any data relating to the structural differences, only an indication that culturing poxviruses (no specific mention of ALVAC or ALVAC(2)) is safer in avian embryonic stem cells cultures. Appendix A cannot support Applicant's assertion that the viruses of Paoletti are different from the instant viruses. Therefore, the rejection is maintained for reasons of record.

7. Claims 15, 22, 23 and 29-31 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Snow (*Bay Area Reporter*, National Institutes of Health: ALVAC Prime and Boost, HIV Vaccine Handbook, Approaches, 1998, pages 201-208). The claims are summarized

above. Snow discloses the general knowledge available to the public regarding ALVAC engineered to express HIV envelope glycoprotein gp120 (page 202). Therefore, the claims are anticipated by Snow's disclosure of the ALVAC/gp120 immunogenic composition administered to humans for treatment of HIV.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the assertion that the compositions have art-recognized structural and functional advantages over previously available compositions. Applicant argues that Snow is completely silent as to the instantly claimed new compositions. Applicant points to Appendix A, evidence that those of skill in the art have noted that the methods described in the instant claims provide a "safer...alternative to the use of...chicken primary embryonic fibroblasts for the production of a large amount of viral vectors and viruses for the manufacture of viral vaccines, such as poxviruses...." Applicant argues that the instantly claimed products have significant structural and functional advantage over previously available products.

In response to Applicant's arguments, the Office has considered Appendix A. Appendix A does not provide any specifics regarding the structural and functional differences between poxviruses produced in CEF cultures versus avian embryonic stem cells cultures. Appendix A only indicates that the use of avian embryonic stem cells cultures is safer. Safer culturing methods do not render the final products any different than ALVAC viruses produced via other means. Although Snow does not disclose the method of production, the final product is an ALVAC virus comprising a gene expressing gp120. Applicant does not appear to have any evidence that the ALVAC and ALVAC(2) viruses of Snow are any different (structurally and

functionally) than the instantly claimed viruses. There does not appear to be any data relating to the structural differences, only an indication that culturing poxviruses (no specific mention of ALVAC or ALVAC(2)) is safer in avian embryonic stem cells cultures. Appendix A cannot support Applicant's assertion that the viruses of Snow are different from the instant viruses. Therefore, the rejection is maintained for reasons of record.

8. (*New Rejection*) Claims 15, 18, 22, 23, 29, 30 and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Schlom *et al.* (US Patent 6,156,460, "Schlom"). The claims are summarized above. Schlom discloses recombinant viral vectors, such as canarypox virus (also called ALVAC) vectors that express prostate specific antigen (col. 2, lines 32-36, and col. 3, lines 5-10). The vectors are administered to subjects to induce an immune response against prostate specific antigen. Schlom discloses that a booster following the initial immunization may be administered using the same pox virus vector, the same antigen, and a co-stimulatory molecule, such as B7.1, which serves as a biological adjuvant. The co-stimulatory molecule is administered via insertion of the gene encoding B7.1 into the recombinant pox vector (columns 5-6, bridging paragraph).

Although Schlom discloses the use of CEF cells for propagating the virus, Schlom's final product is expected to be the same as Applicant's product: an ALVAC virus comprising a gene encoding a tumor antigen and a human co-stimulatory molecule, B7.1. Therefore, Schlom's disclosure anticipates the claimed invention.

Conclusion

9. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 2/2/07

STACY B. CHEN
PRIMARY EXAMINER